REMARKS

1. The Examiner is thanked for indicating that claims 1-10, 13-20, 24, and 65-78 are free of the prior art and in allowable form. Hence, the present amendment is directed to rejected claims 11-12, 21-22 and 27.

2. Claims 11, 12, 21, 22 and 27 were given a "scope"/enablement rejection. In response to the enablement rejection claim 27 has been cancelled, and claims 11 and 12 have been amended to require that the claimed compound be capable of activating MC1 receptors in vitro. Likewise, claim 22 has been amended to recite that the compound is capable of stimulating the in vitro production of IL-8 and/or IL-10.

The rejection of claim 21 is respectfully traversed on the basis of the experimental data set forth in the enclosed declaration, which demonstrates that two of the claimed compounds (MS05 and MS09) have an in vivo effect (in rats) on TNF-α production.

The effect on TNF-α implies that IL-1 and IL-6 will also be affected. Alpha-MSH has been shown to have marked anti-inflammatory effects in vitro and in vivo that includes melanocortin type 1 receptor (MC1) mediated stimulation of the release of the cytokine synthesis inhibitor IL-10 from monocytes (J. Immunol. 156:2517-21, 1996) and downregulation of the synthesis and release of the proinflammatory cytokines IL-1; IL-6 and TNF-α (Immunol. Today 18; 140-45, 1997) as well as the production of NOS mediated NO by macrophages (J. Leukoc Biol 59:248-53, 1996).

Therefore a compound that binds to and activates MC1 receptors with the same or higher affinity and efficacy as aMSH and had proven effective in order to reduce LPS induced TNFα production in a similar or even more pronounced way than aMSH, will also have the ability to inhibit LPS induced IL-1 and IL-6 production.

Both MS05 and MS09 fulfils these criteria since both

peptides have binding affinities for the MC1 receptor that are comparable with aMSH and both peptides have the same maximal efficacy on MC1 receptor activation as aMSH (Peptides 21, 239-43, 2000).

Also, an effect on TNF-α by itself would necessarily result in decreased production of nitric oxide and down-regulation of NOS activity. It is well-known that inducible nitric oxide synthase (iNOS) is transcriptionally induced by bacterial constituents and inflammatory mediators, including TNF-α and IL-1. It is therefore logical that a peptide such as MS05 or MS09 which has the ability to inhibit LPS induced TNF-α liberation will also inhibit NOS activity and thereby NO accumulation.

We have also presented new claims. Claim 79-82 are based on claim 21, but recite only in vitro effects, and claim 83 only recites decreasing the formation of TNF-alpha.

3. In response to the indefiniteness rejection, claim 6 has been rewritten in independent form.

Respectfully submitted,

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Enclosure
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